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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,025	10/19/2006	Dennis L. Panicali	701281	3646

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EXAMINER	
SHEN, WU CHENG WINSTON	
ART UNIT	**PAPER NUMBER**
1632	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/579,025	PANICALI ET AL.	
	Examiner	Art Unit	
	WU-CHENG Winston SHEN	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *2-5 and 23-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 6-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :05/11/2006, 07/09/2008, and 04/07/2009.

DETAILED ACTION

This application 10/579,025 filed on 10/19/2006 is a 371 of PCT/US2004/038643 filed on 11/12/2004 which claims benefit of 60/519,354 filed on 11/12/2003.

Election/Restriction

Applicant's election with traverse of Group I, claims 1 and 6-22, drawn to a method for inducing an immunological response against a malignant pancreatic cell in an individual, said method comprising the steps of: selecting an individual having malignant pancreatic cells or at risk for developing such a pancreatic tumor, administering to the individual a first vector containing a first gene, or antigenic portion thereof, that encodes a pancreatic tumor-associated antigen (PTAA), and at regular intervals thereafter administering at least a second vector containing a gene encoding PTAA or antigenic portion thereof, wherein the PTAA is selected from the group consisting of carcinoembryonic antigen (CEA), mucin (MUC), ras, gastrin, erbB2, interferonα, tumor necrosis factor-α, hMP-9 immunotoxin, antigenic portions thereof, and modified versions thereof, with the specific combination of (i) a first PTAA being carcinoembryonic antigen (CEA) and (ii) a second PTAA being mucin (MUC), in the reply filed on 02/25/2009 is acknowledged. Furthermore, in response to the requirement for species election, Applicants elect, with traverse, the following: Species (i) an orthopox virus vector as recited in claim 7; Species (ii) MUC-1 as recited in claim 12; Species (iii) MVA as recited in claim 20; and Species (iv) MUC-1 as recited in claim 24. All of the claims of elected Group I read on the elected Species (i)-(iii). Applicants note that only claims 23-25 of non-elected Group

III read on the elected Species (iv); however, a species selection of Species (iv) was included for the sake of completeness.

The traversal is on the ground(s) that (1) Applicants believe that the subject matter of the claims of at least Groups I and II are linked so as to form a single general inventive concept. In other words, the claims of Groups I and II share a common special technical feature, which defines the contribution that each claim makes over the prior art. In this respect, the claims of Groups I and II are directed to a method for inducing an immunological response comprising administering to an individual with malignant pancreatic cells or at risk for developing a pancreatic tumor (i) a first vector encoding a PTAA and (ii) subsequently administering a second vector encoding a PTAA; and (2) Given the special technical feature common to the claims of Groups I and II, a search for prior art with respect to either Group I or Group II would likely uncover references that would be considered by the Examiner during the examination of the other group. As a result, the Examiner would incur no undue burden in examining the claims of both Group I and Group II at the same time.

The traversal is not found persuasive because (1) As stated in the Requirement for Restriction mailed on 11/25/2008, Applicant's claims encompass multiple inventions, multiple products (nucleic acid and protein) and multiple methods (methods of using the products for inducing immunological response), and do not have a special technical feature which link the inventions one to the other, and lack unity of invention. The common technical feature in all groups is a MUU-1 polypeptide encoded by a nucleic acid molecule. However, this common technical feature cannot be a special technical feature under PCT Rule 13.2 because the feature is shown in the prior art. **Taylor-Papadimitriou et al.** teaches that the MUC1 membrane mucin

was first identified as the molecule recognized by mouse monoclonal antibodies directed to epithelial cells, and the cancers which develop from them (See abstract, Taylor-Papadimitriou et al., MUC1 and cancer, *Biochim Biophys Acta.* 1455(2-3):301-13, 1999); (2) Group II is distinct from Group I because the method steps of Group II require administration of granulocyte-macrophage colony stimulating factor (GM-CSF) as a co-stimulatory molecule whereas the method steps of Group I do not require administration of granulocyte- macrophage colony stimulating factor (GM-CSF) as a co-stimulatory molecule. The search for claims in Group I-II is distinct one from each other and not co-extensive and thereby presents search burdens on the examiner. It is further noted, however, that search burden is not germane to PCT lack of unity practice.

Claims 1-44 are pending.

Claims 2-5 and 23-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 01/29/2009.

Claims 1 and 6-22 are currently under examination to the extent of the specific combination of (i) a first PTAA being carcinoembryonic antigen (CEA) and (ii) a second PTAA being mucin (MUC), and the following elected species: an orthopox virus vector as recited in claim 7; MUC-1 as recited in claim 12; and MVA as recited in claim 20

The requirement is still deemed proper and is therefore made FINAL.

Claim Objections

1. Claims 1 and 6-22 are objected to for being drawn to a non-elected invention. Specifically, Applicants have elected the specific combination of (i) a first PTAA being carcinoembryonic antigen (CEA) regarding a first vector containing a first gene, or antigenic portion thereof, that encodes a pancreatic tumor-associated antigen (PTAA) recited in claim 1, and (ii) a second PTAA being mucin (MUC) regarding a second vector containing a gene encoding PTAA or antigenic portion thereof recited in claim 1; and as such, claim 1 and dependent claims 6-22 are examined only to the extent that they read on the specific combination of (i) a first PTAA being carcinoembryonic antigen (CEA) and (ii) a second PTAA being mucin (MUC). Applicants are required to delete the non-elected subject matter from the instant claim by claim amendments.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1 and 6-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Laidlaw et al.** (U.S. patent 7,273,605, issued date 09/25/2007, effective filing date 11/30/2001) in view of **Pecher** (WO 01/24832, PCT/DE00/03443, filed on 09/26/2000; this document is cited as reference AA in the IDS filed by Applicant on 07/09/2008), and **Kotera et al.** (Kotera et al.,

Humoral immunity against a tandem repeat epitope of human mucin MUC-1 in sera from breast, pancreatic, and colon cancer patients. *Cancer Res.* 54(11):2856-60, 1994).

Claim 1 is directed to a method for inducing an immunological response against a malignant pancreatic cell in an individual, said method comprising the steps of: selecting an individual having malignant pancreatic cells or at risk for developing such a pancreatic tumor, administering to the individual a first vector containing a first gene, or antigenic portion thereof, that encodes a pancreatic tumor-associated antigen (PTAA), and at regular intervals thereafter administering at least a second vector containing a gene encoding PTAA or antigenic portion thereof, wherein the PTAA is selected from the group consisting of carcinoembryonic antigen (CEA), mucin (MUC), ras, gastrin, erbB2, interferonα, tumor necrosis factor-α, hMP-9 immunotoxin, antigenic portions thereof, and modified versions thereof, with the specific combination of (i) a first PTAA being carcinoembryonic antigen (CEA) and (ii) a second PTAA being mucin (MUC). Claims 11-16 limit to the recited carcinoembryonic antigen (CEA), and further limit antigen to various recited mucins (MUC). Claims 6-10, and 17-21 further limit to specified orthopox vector and avipox vector for expression of PTAAs [i.e. carcinoembryonic antigen (CEA) and mucin (MUC)]. Claim 22 further limits to recited set interval for administration.

Laidlaw et al. teaches a method which comprises administering a priming composition (which comprises a first non-replicating viral vector) and a boosting composition (which comprises a second non-replicating viral vector) to a subject to treat and/or prevent a cancer.

Laidlaw et al. teaches a viral particle comprising such a genome and its use to deliver a nucleotide of interest (NOI) to a target cell, and a fowlpox virus genome which has modifications in one or more wild-type FPV genes (See abstract, lines 5-10 of column 2, lines 57-60 of column 13, Laidlaw et al.).

With regard to the limitations pertaining to poxvirus, orthopox virus, avipox vector, and MVA recited in claims 6-10, and 17-21 of instant application, Laidlaw et al. teaches poxviruses have been exploited as recombinant vectors for the heterologous expression of foreign proteins. In particular, recombinant vaccinia virus has been studied as a tool for transient expression of genes in mammalian cells and an experimental recombinant vaccine vector (See lines 17-22, column 1, Laidlaw et al.). Laidlaw et al. teaches the family of poxviruses can be split into two subfamilies, the *Chordopoxvirinae* and the *Entomopoxviriniae*. The *Chordopoxvirina*e (poxviruses of vertebrates) include geni of orthopoxviruses and avipoxviruses. In a preferred embodiment the present invention provides a vaccine, priming or boosting composition which comprises a non-replicating pox virus vector. (See lines 41-50, column 6, Table 2, Laidlaw et al.). Laidlaw et al. teaches that concern about the capacity of vaccinia virus to replicate in mammalian cells has limited its clinical use and led to the search for safer alternatives, and these include attenuated vaccinia viruses, such as modified vaccinia Ankara (MVA) (See lines 38-41, column 1, Laidlaw et al.).

With regard to the limitation orthopox vector is administered before the avipox vector is administered recited in claim 21, Laidlaw et al. teaches that the two viral vectors maybe derived from viruses belonging to the same family (such as pox viruses) but different geni (e.g. the

genus of orthopoxviruses and the genus of avipoxviruses) (See lines 40-47, column 7, Laidlaw et al.).

With regard to the limitation the limitation the set interval is 20 days to 90 days, recited in claim 22, Laidlaw et al. teaches various prime-boost immunization regimes using with different poxvirus vectors, such as 3-4 weeks intervals (See Example 14, columns 31-32, Laidlaw et al.).

With regard to carcinoembryonic antigen (CEA), mucin (MUC) as tumor associated antigens, Laidlaw et al. teaches nucleotide of interest (NOI) may, for example, be or encode one of the following: an antigen, cytokines, immune co-stimulatory molecules, immunomodulatory molecules. In one preferred embodiment, the NOI is capable of encoding a disease (e.g. cancer) associated antigen. Exposure to an antigen in the context of a fowlpox vector may provoke or boost immune responses to the antigen such that an existing or subsequent challenge is dealt with more effectively. (See lines 37-53, column 13, Laidlaw et al.). Laidlaw et al. teaches the target antigen may be an antigen which is recognized by the immune system after infection with the disease; and for cancers, preferred colon cancer antigens: CEA, MUC-1, MAGE-12, mutant P53 whereas preferred breast cancer antigens are MUC-1, HER2, CEA (See lines 19-30, column 20, Laidlaw et al.). Laidlaw et al. teaches number of other compositions may be employed in heterologous vaccination programs. If the genome/particle of the present invention comprises an NOI (optionally capable of encoding a POI, protein of interest), then preferably the other composition comprises the same NOI or POI. Other compositions, in addition to pox virus vectors, include "naked DNA", non-viral vector systems and other viral vector systems,

and naked DNA (or RNA) may be linear or circular (for example, a plasmid). (See lines 48-57, column 14, Laidlaw et al.).

Laidlaw et al. does not explicitly teach a first pancreatic tumor-associated antigen (PTAA) being carcinoembryonic antigen (CEA) and a second PTAA being mucin (MUC).

Pecher teaches a pharmaceutical composition for treating and preventing human tumors, which express the tumor antigen carcinoembryonic antigen (CEA) and the tumor antigen mucin, and to the use thereof as a vaccine in humans for activating the immune system. The pharmaceutical composition is provided comprising a plasmid which contains the gene for the human carcinoembryonic antigen (CEA) SEQ No. 2., and another plasmid which contains the human mucin gene MUC1, active fragments thereof or at least 3 repeats of amino acid sequence SEQ No. 1, which reads on wobble MUC-1 or wobbled mini-MUC recited in claim 16 of instant application (See abstract, Pecher, W/O 01/24832, 2000).

Kotera et al. teaches humoral immunity against a tandem repeat epitope of human mucin MUC-1 in sera from breast, pancreatic, and colon cancer patients.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time of the invention to combine the teachings of Laidlaw et al. regarding a method which comprises administering a priming composition (which comprises a first non-replicating viral vector) and a boosting composition (which comprises a second non-replicating viral vector) to a subject to treat and/or prevent a cancer; a viral particle comprising such a genome and its use to deliver a nucleotide of interest (NOI) to a target cell, and a poxvirus vector or a plasmid for expression of NOI; and both CEA and MUC-1 being preferred colon cancer antigens as well as

breast cancer antigens, with (i) the teachings of Pecher regarding the pharmaceutical composition is provided comprising a plasmid which contains the first gene for the human carcinoembryonic antigen (CEA), and a second plasmid which contains the human mucin gene MUC1, active fragments thereof, and (ii) the teachings of Kotera et al. regarding humoral immunity against a tandem repeat epitope of human mucin MUC-1 in sera from breast, pancreatic, and colon cancer patients, to arrive at the claimed methods for method for inducing an immunological response against a malignant pancreatic cell in an individual, comprising the recited steps.

One having ordinary skill in the art would have been motivated to combine the teachings of Laidlaw et al., Pecher, and Kotera et al. because (i) Pecher explicitly teaches a pharmaceutical composition for treating and preventing human tumors, which express the first tumor antigen carcinoembryonic antigen (CEA) from the first plasmid vector and the second mucin (MUC) from the second plasmid vector, and to the use thereof as a vaccine in humans for activating the immune system, (ii) Laidlaw et al. teaches a poxvirus vector or a plasmid vector for the expression of CEA and MUC-1, which are established tumor associated antigens (TAAs) for colon and breast cancers, and (iii) Kotera et al. teaches humoral immunity against a tandem repeat epitope of human mucin MUC-1 in sera from pancreatic, colon, and breast cancer patients.

There would have been a reasonable expectation of success given (i) successful establishment of various prime-boost immunization regimes for clinical trials using combination of poxvirus vectors each expresses a NOI, which encodes a polypeptide or an antigenic determinant that induces immunological response in an individual, and CEA and MUC-1 are preferred tumor associated antigens for immunization, by the teachings of Laidlaw et al., (ii) a

pharmaceutical composition for treating and preventing human tumors, which express the tumor antigen carcinoembryonic antigen (CEA) and express the tumor antigen mucin, and to the use thereof as a vaccine in humans for activating the immune system, and the pharmaceutical composition comprising the first plasmid which contains the gene for the human carcinoembryonic antigen (CEA) SEQ No. 2., and the second plasmid which contains the human mucin gene MUC1, by the teachings of Pecher, and (iii) humoral immunity against a tandem repeat epitope of human mucin MUC-1 in sera from breast, pancreatic, and colon cancer patients, by the teachings of Kotera et al.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Conclusion

3. No claim is allowed.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent

examiner, Peter Paras, Jr. can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Wu-Cheng Winston Shen/

Patent Examiner
Art Unit 1632